

Build Better Biologics with Machine Learning and Synbio

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April 10, 2019



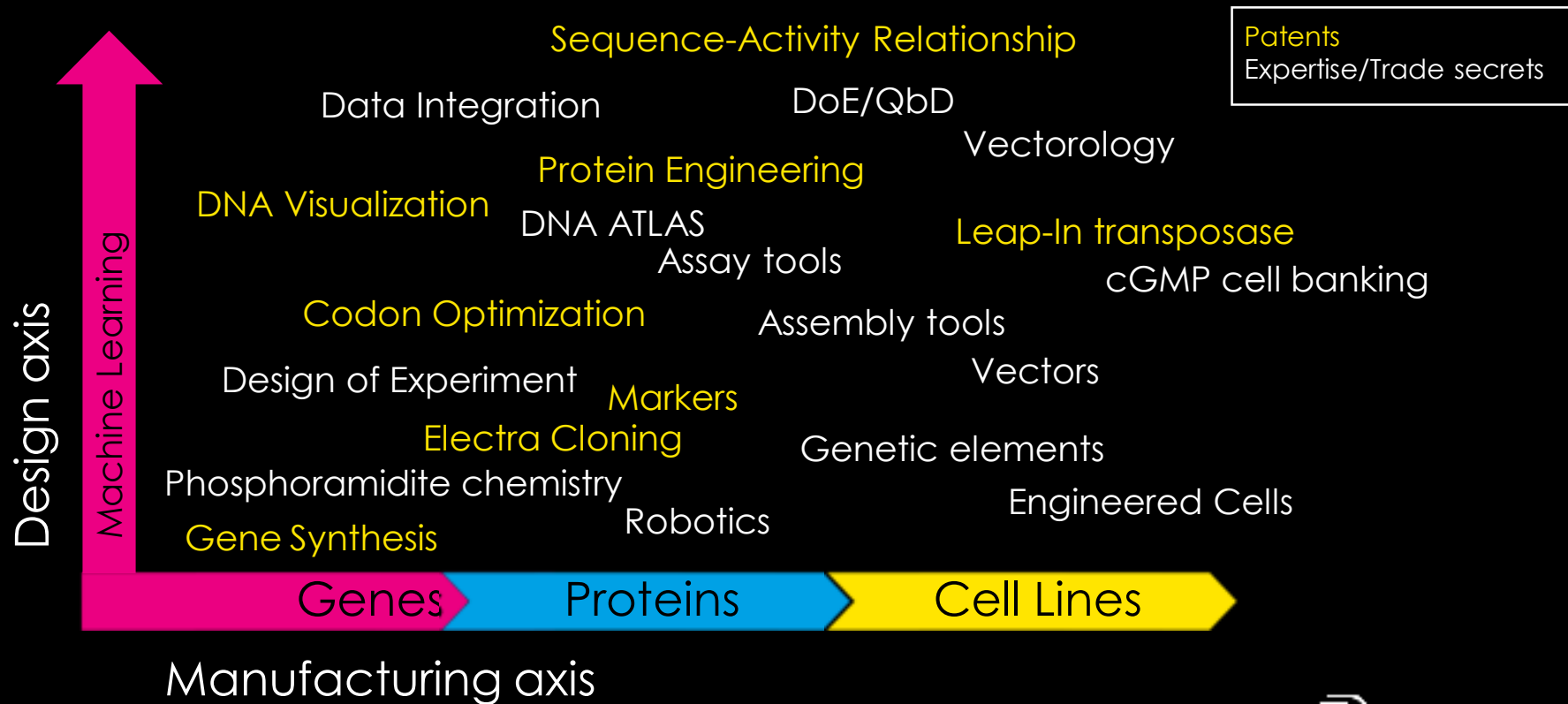


-
- Founded in 2003
 - Based in SF Bay Area
 - ~100 Employees

- 23 issued patents
- >60 peer-reviewed papers
- Rebranded to **ATUM** 2016



Ecosystem of Integrated Tools

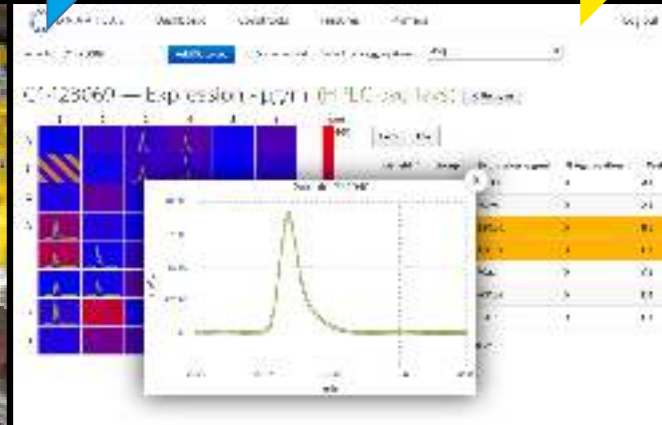


High Throughput Biologics Automation

Genes

Proteins

Cell lines



Mammalian Protein Expression



Transient Expression

Speedy Pools

Stable Expression

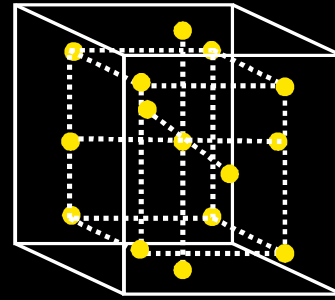
>20,000 protein lots

mg to 30 gram

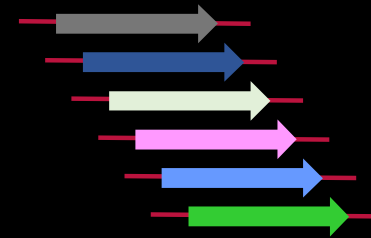
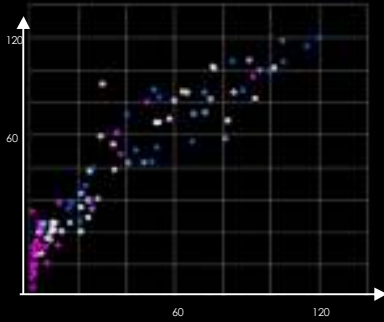
Full analytics

Design of Experiment

Genomic Data

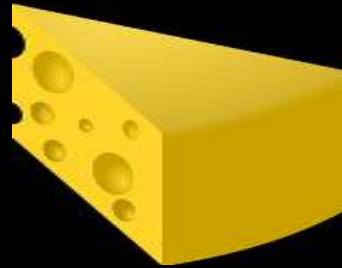


Machine Learning



Synthetic Biology

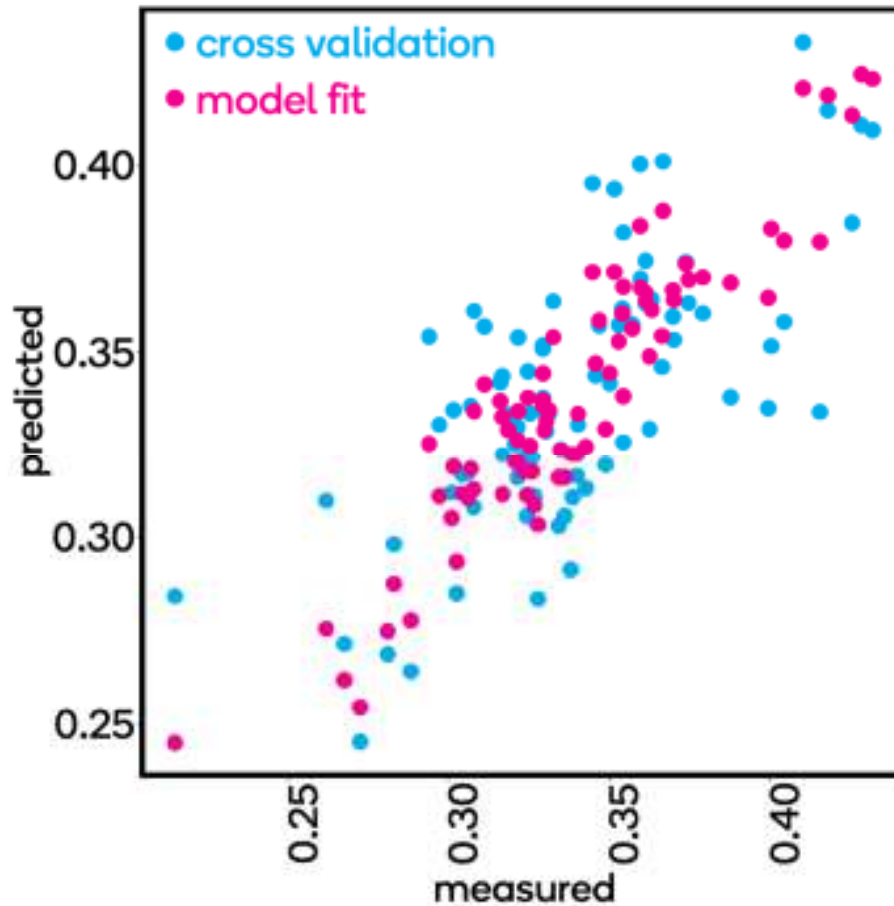
Drug Candidate



Biology

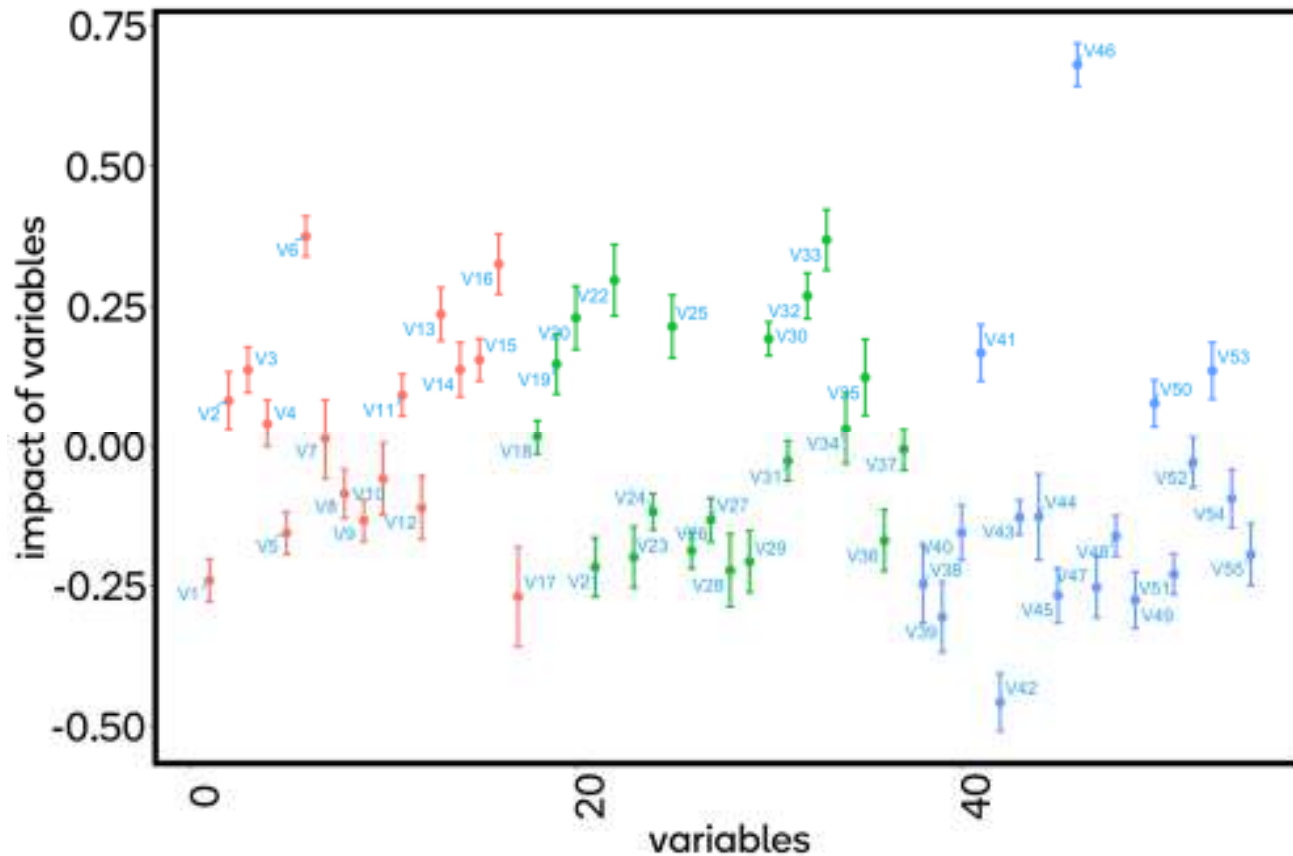


Machine Learning Models



- Consensus Models from several algorithms
- Models for every measured attribute
- Models on fitness functions
- Cross-validated leaving 15% out
- Only ~96 variants per round

Machine Learning Models



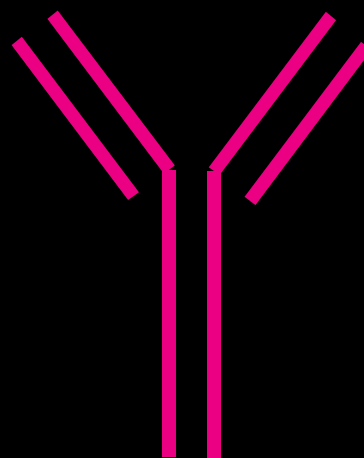
Captures additivity and epistasis
Impact of substitutions quantified.
~ 10^{20} Sequence Space explored

Case Study: Testing 184 Variants To Capture the Space of 10^{23} Variants

Total available space:

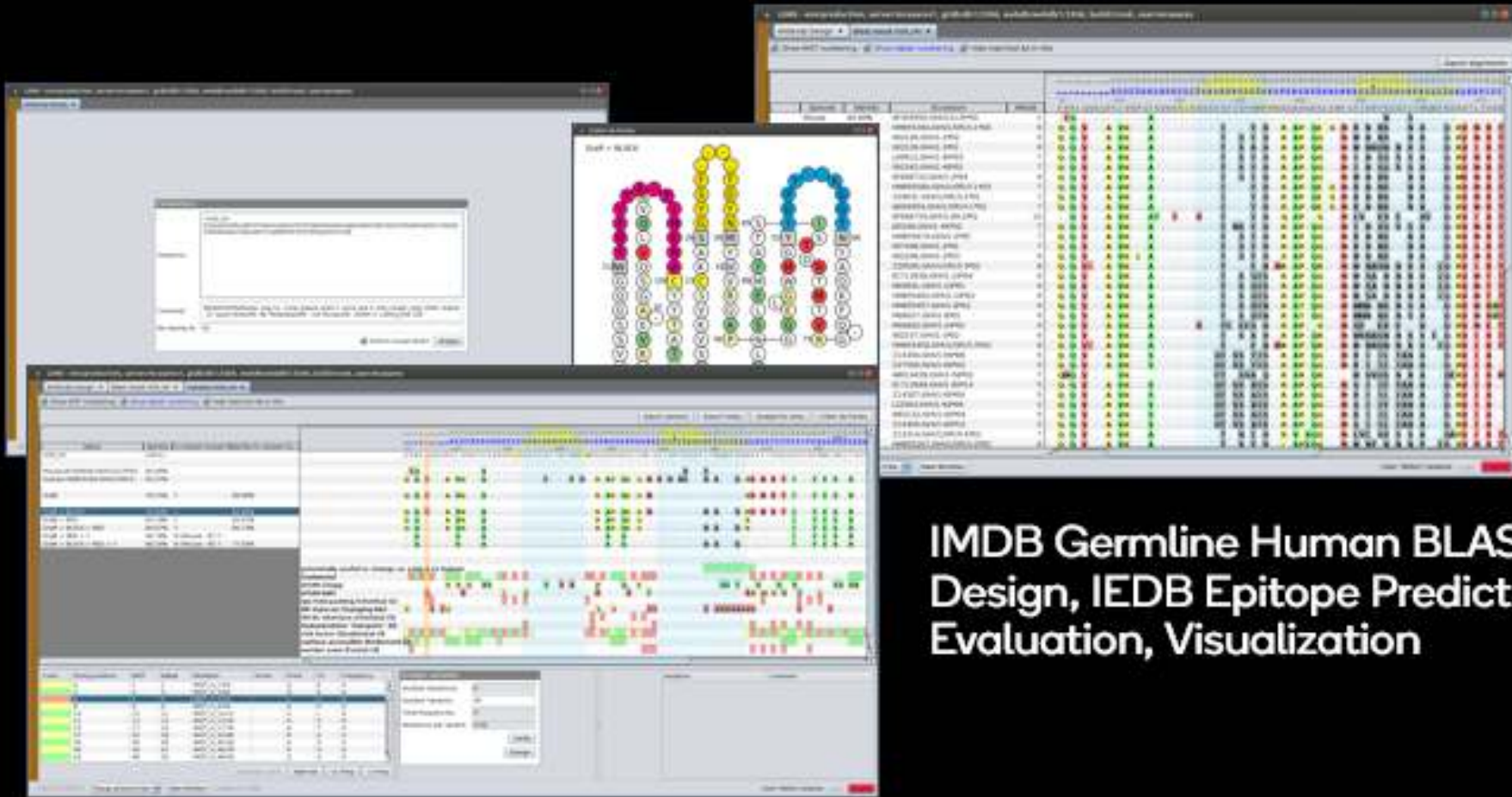
$$V_H = 2^{41} (\sim 10^{12})$$

$$V_L = 2^{36} (\sim 10^{10})$$



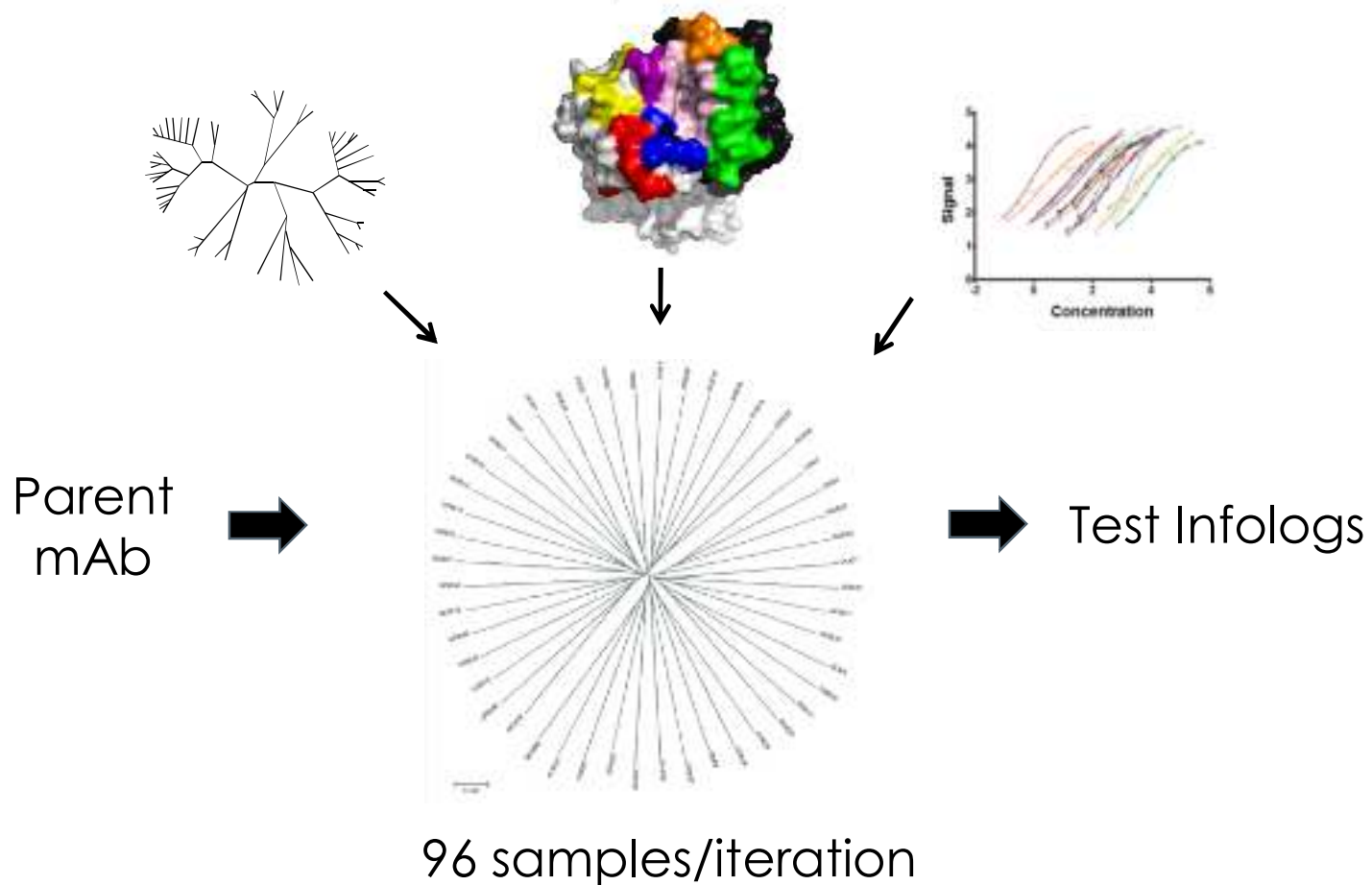
Starting from commercial molecule

Biotech is Data Management

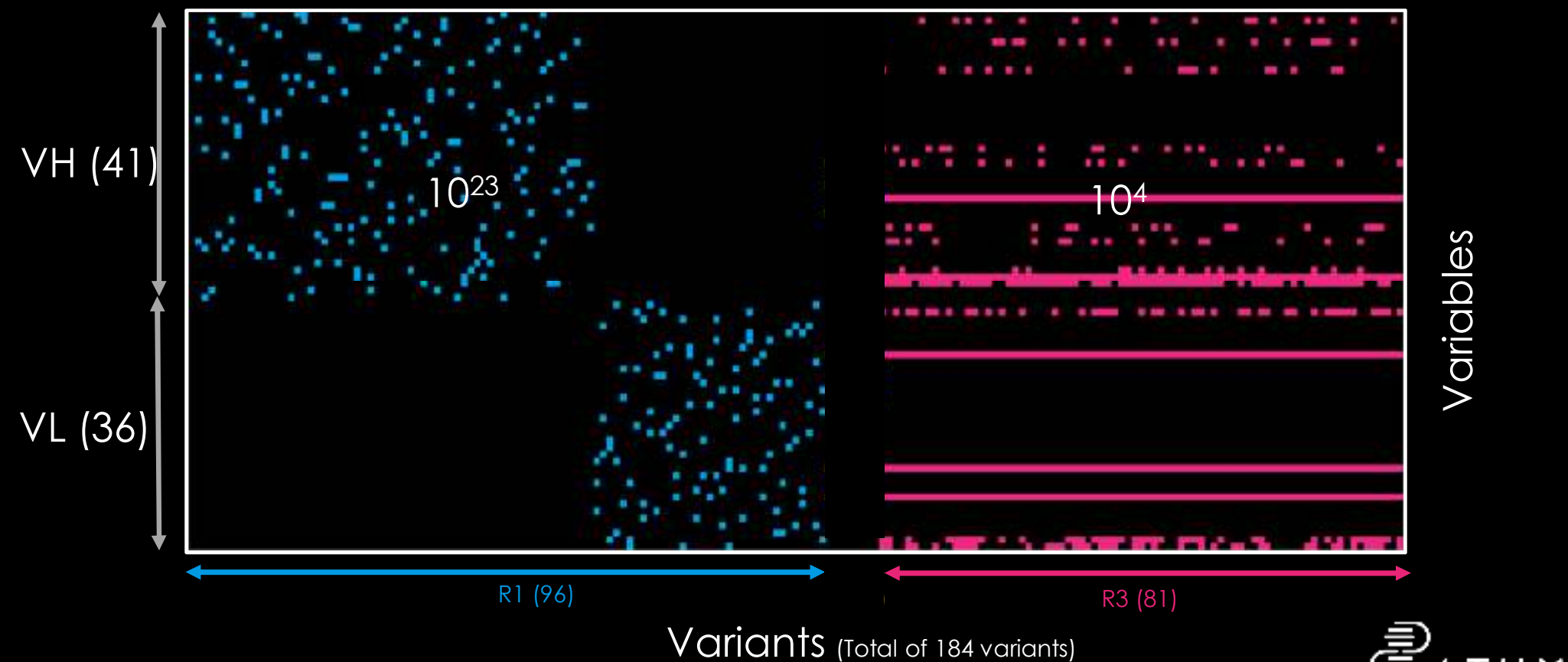


IMDB Germline Human BLAST, DOE Design, IEDB Epitope Prediction, Evaluation, Visualization

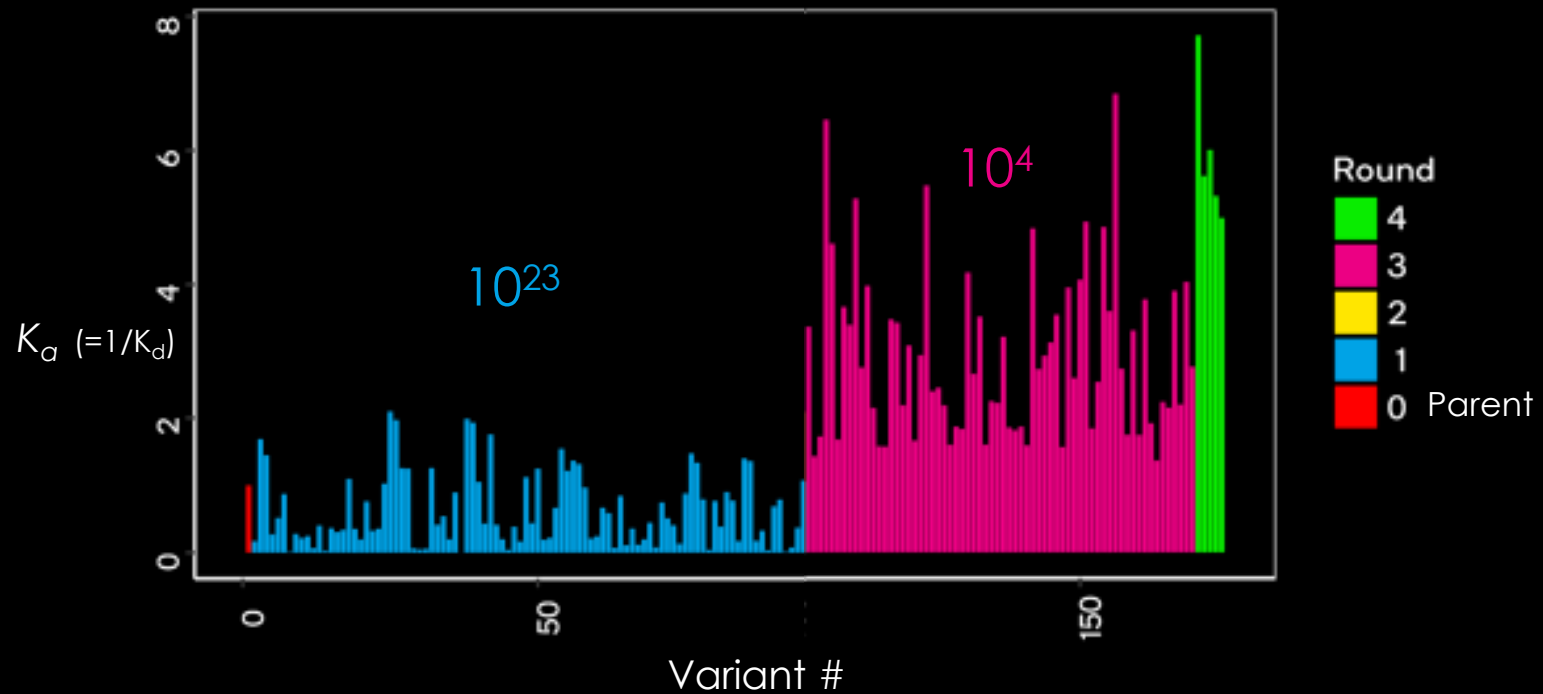
Variable Selection and Library Design



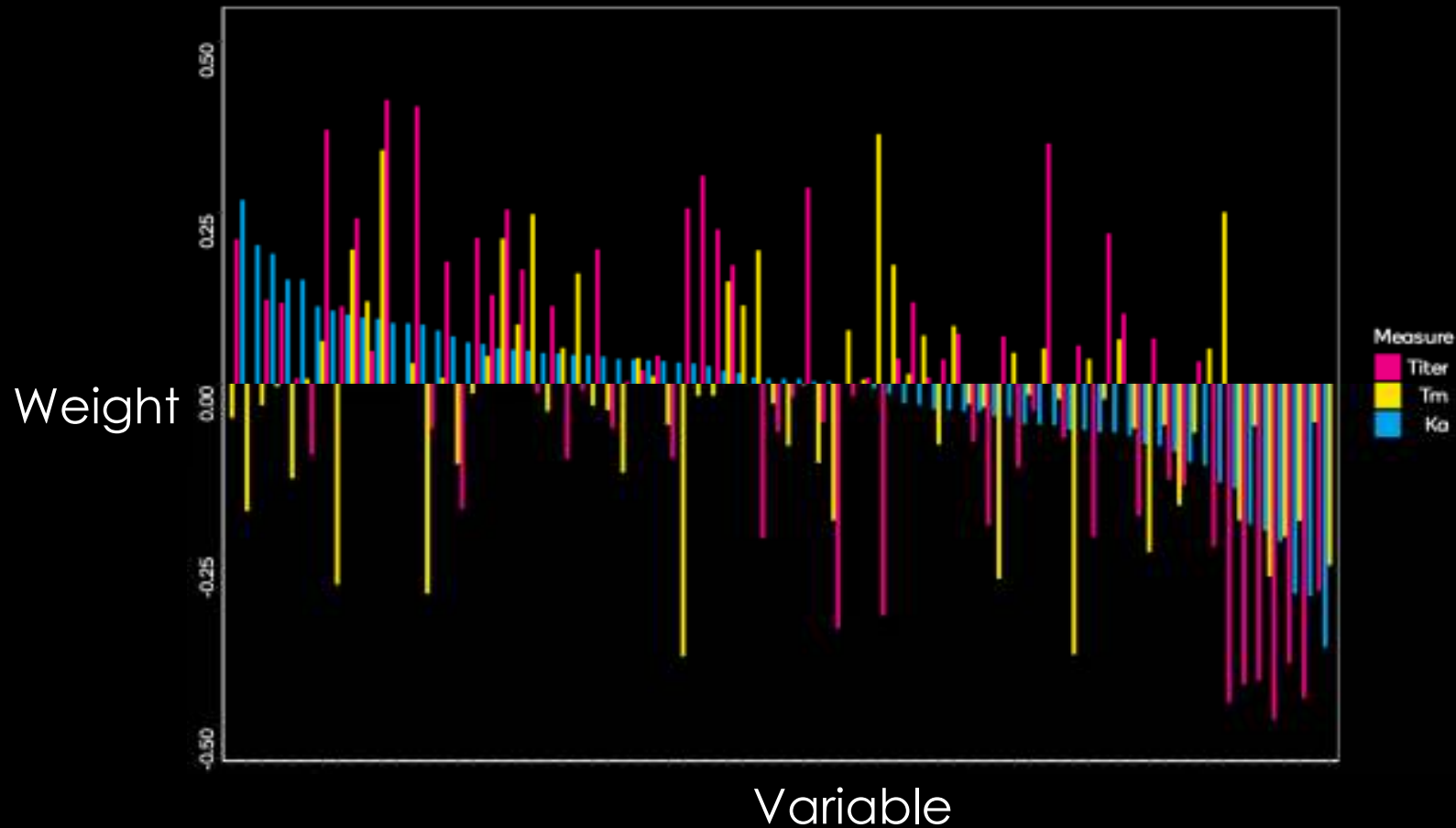
Variable Matrix



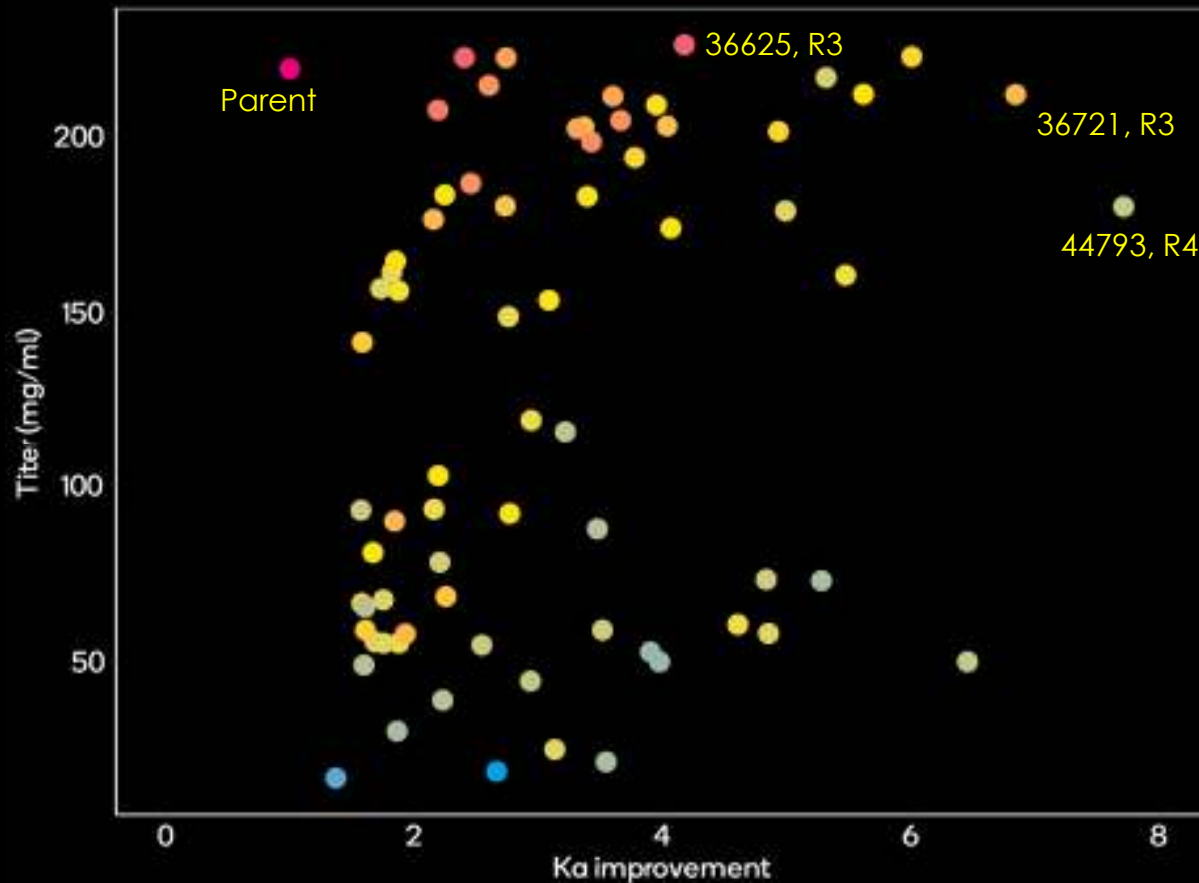
K_d Improvement by Round



Multidimensional Variable Weight Plot



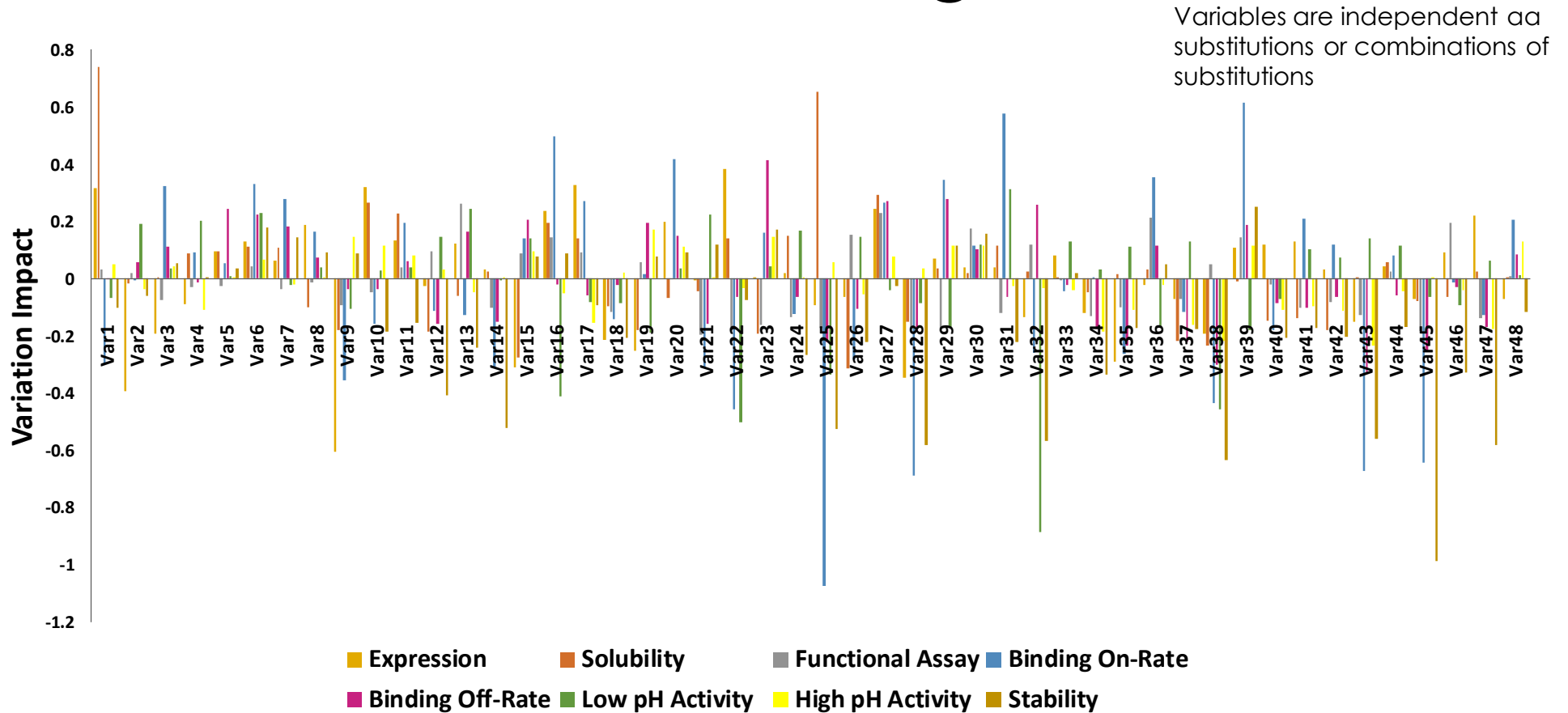
Multi-Dimensional Improvements



Clone	Titer (mg/L)	Tm (°C)	Kd (nM)
36721	212	59	0.16
36625	226	62	0.25
44793	180	56	0.14
Parent	219	63	0.98



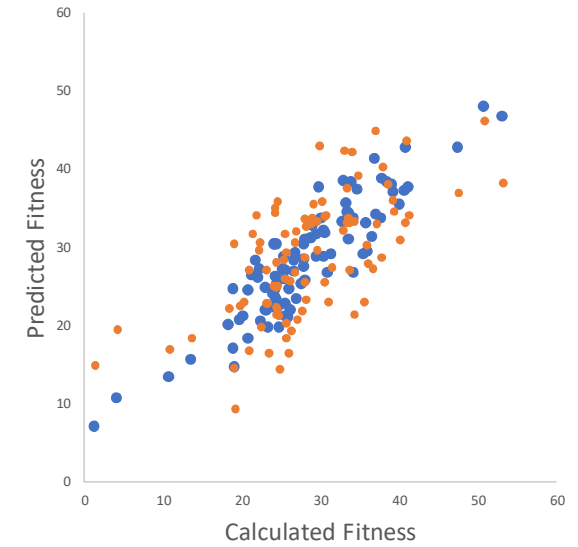
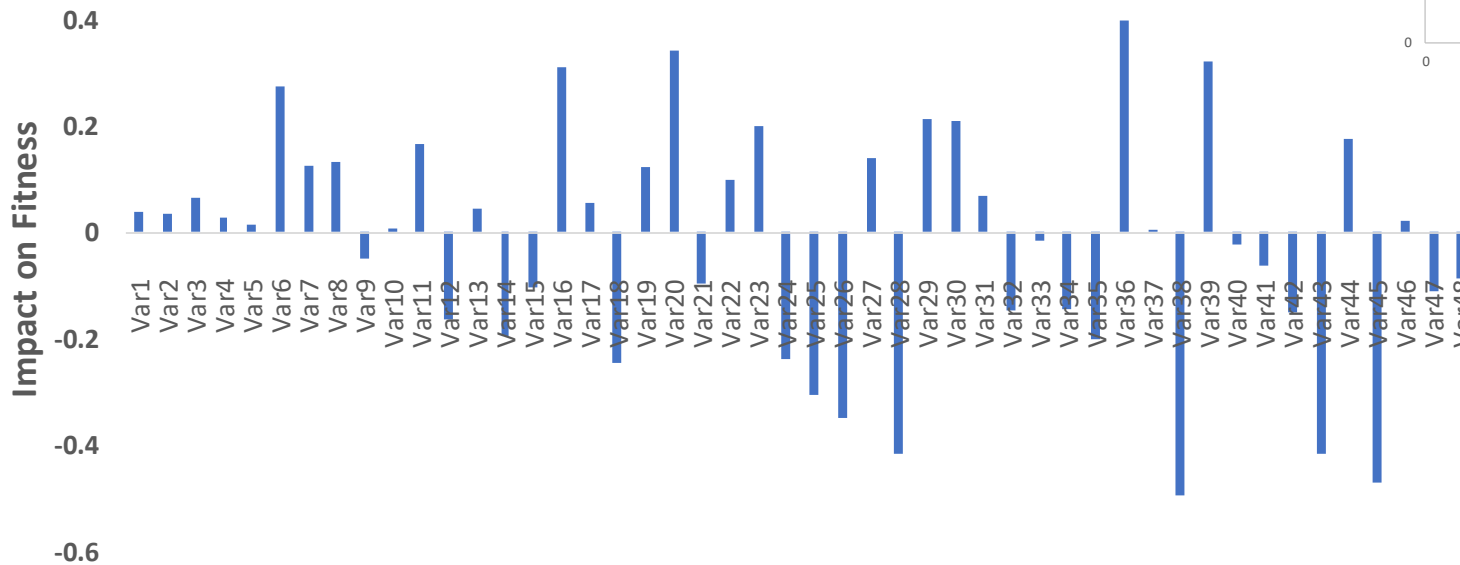
Multi-Functional Modeling



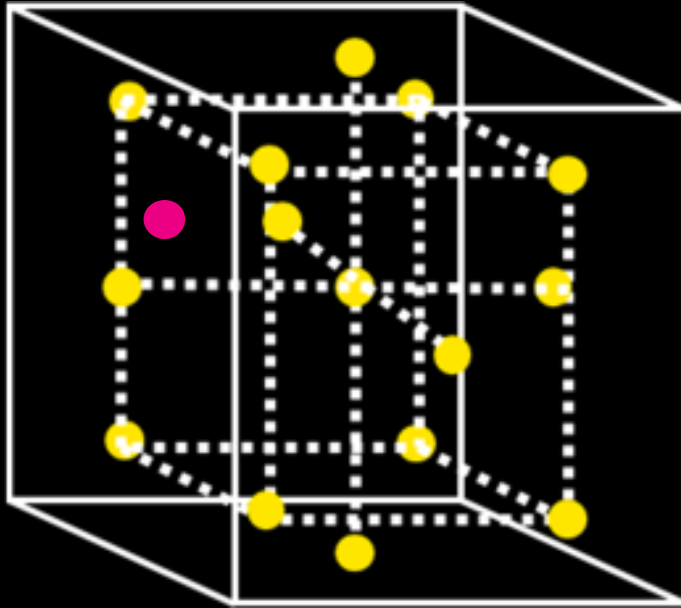
Multi-Dimensional Fitness

Fitness =
6x Function A
1x Function B
3x Function C
5x Function D
2x Function E
2x Function F
5x Function G
5x Function H

Variations are independent
substitutions or combinations



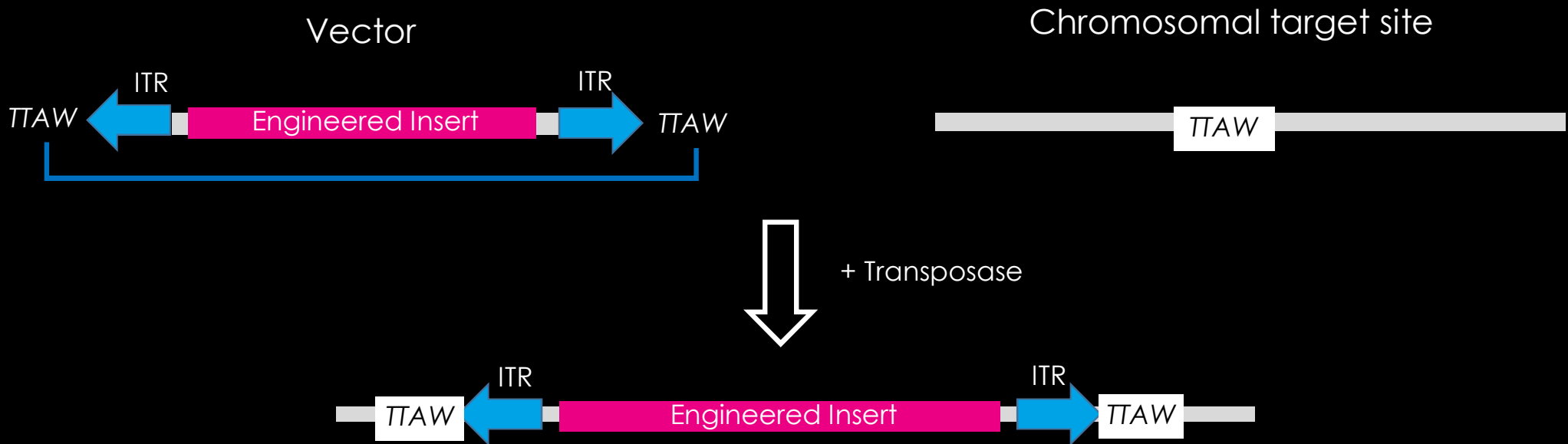
Life is Multidimensional



Winner

- ✓ Cell based assay
- ✓ Antigen binding
- ✓ SEC HPLC
- ✓ Tm stable
- ✓ Humanized
- ✓ 'AdiMab 7'
- ✓ ...And more

Leap-In® Mediated Integration



- Single copy integration at each site
- Multiple insertions across the genome

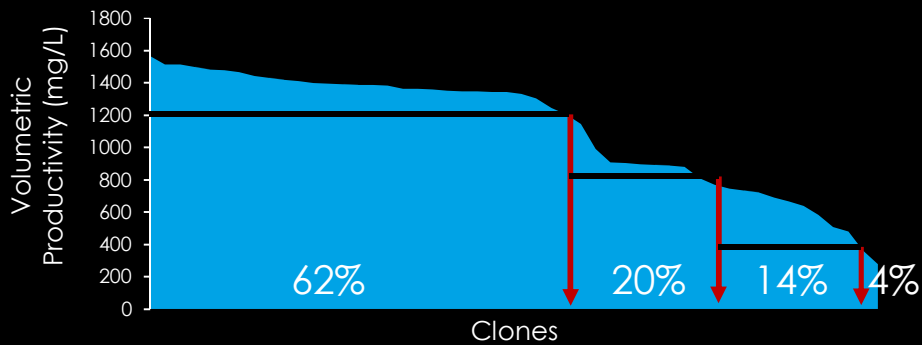
W = A or T
2 Transposases



Robust High Titters Fast

High productivity stable pools

Clonal distribution in Leap-In transposase® mediated stable pools



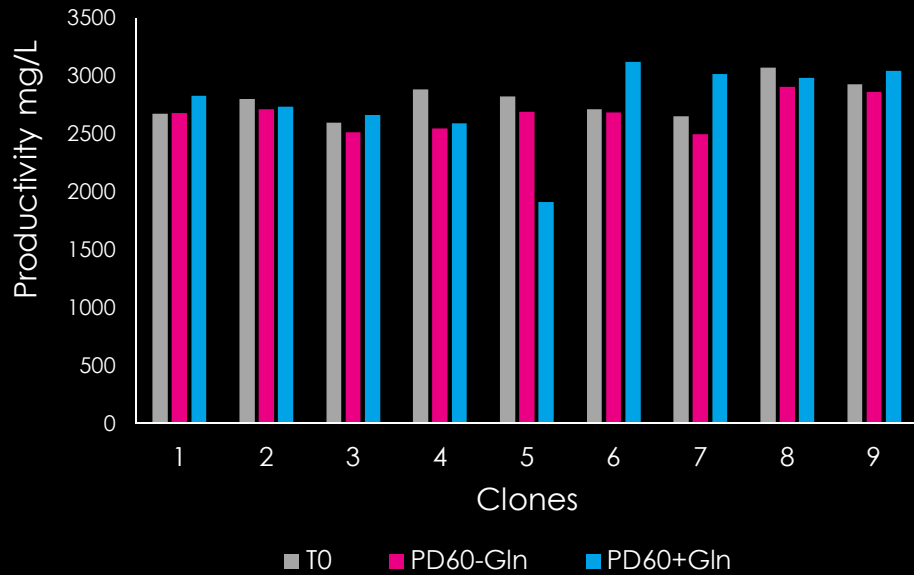
- 62% of clones in top quartile of expressers
- 82% of clones in top half of expressers

Representative Pool Titters

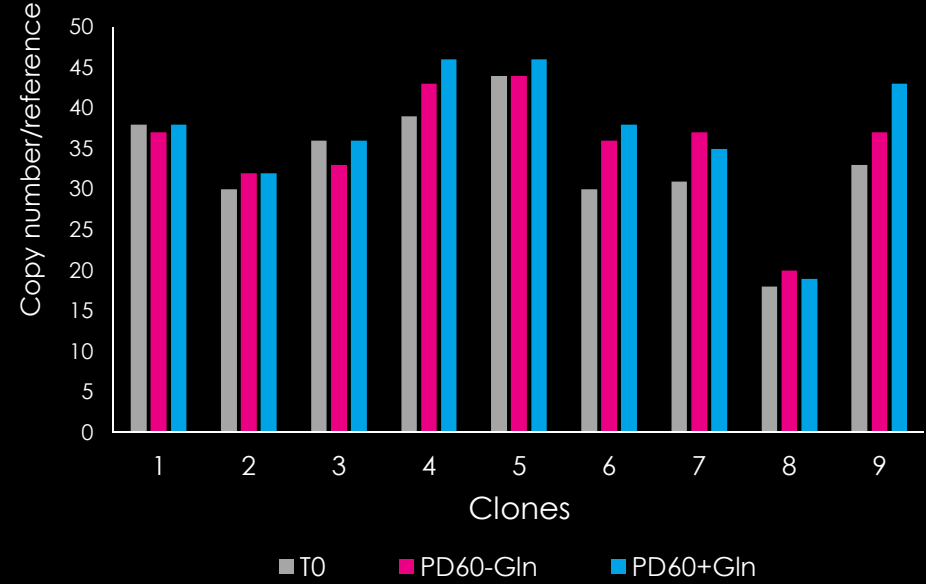
Protein	Volumetric productivity	Specific productivity
IgG1	4.2 g/L	42 pcd
IgG1	3.6 g/L	29 pcd
IgG1	3.3 g/L	29 pcd
IgG1	2.8 g/L	30 pcd
IgG1	4.2 g/L	33 pcd
IgG4	5.0 g/L	43 pcd
IgG4	5.0 g/L	49 pcd

Highly Stable Clones

Productivity stability

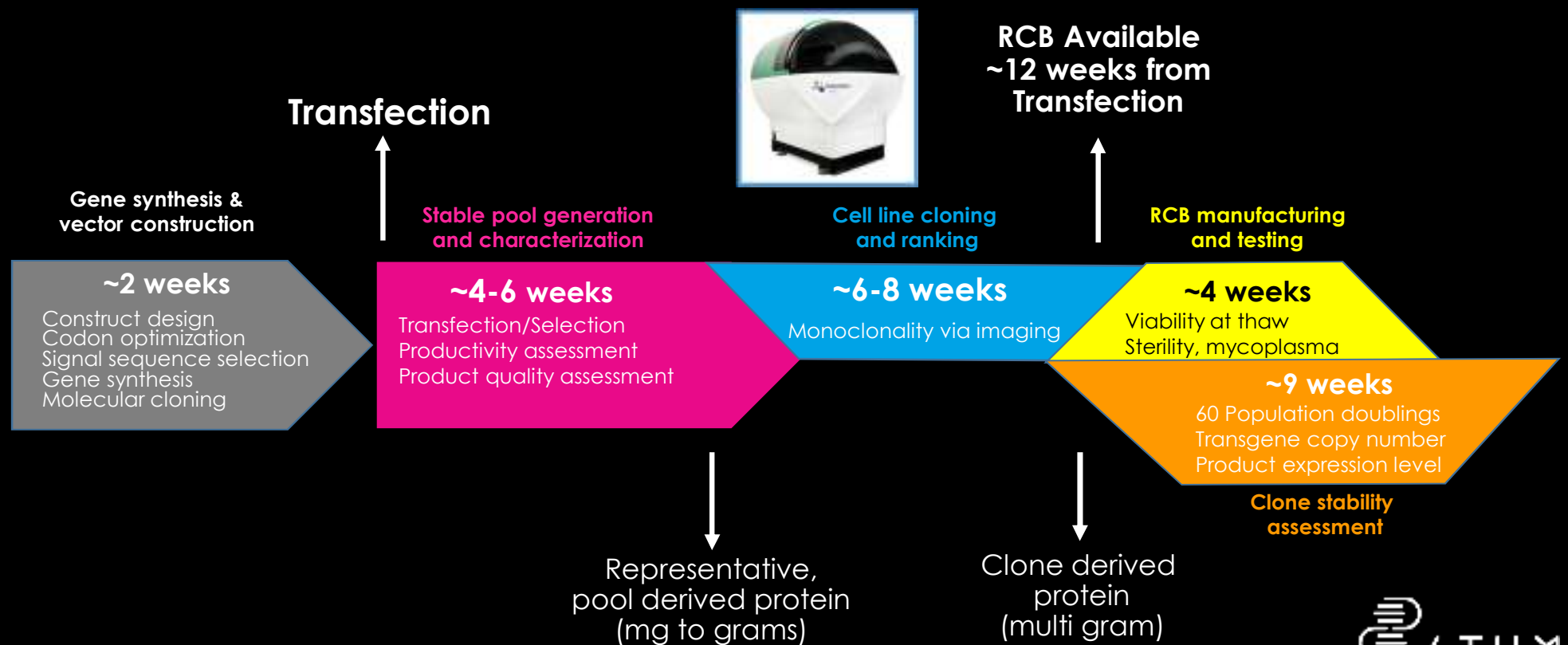


Copy number stability



Timeline

Transfection to RCB in 12 weeks



Thank You



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Technology presented is protected by issued US patents 10233454, 10041077, 9771402, 9580697, 9574209, 9534234, 9493521, 9428767, 9290552, 9206433, 9102944, 8975042, 8825411, 8635029, 8412461, 8401798, 8323930, 8158391, 8126653, 8005620, 7805252, 7561973, 7561972 and pending applications

